## REMARKS

These remarks are responsive to the Office action dated August 11, 2006 on the above-identified patent application. Claims 34 and 36-47 are pending in the application. Claims 34 and 36-47 stand rejected. The rejections are addressed below.

### I. 35 U.S.C. § 103

Claims 34 and 36-47 stand rejected under 35 U.S.C. § 103 as allegedly unpatentable over Lam et al., 1991, *Nature* 354:82 (hereinafter "Lam"); and Egner et al. 1997, *Chem. Commun.* 735 (hereinafter "Egner"); and U.S. Patent No. 4,053,433 (hereinafter "Lee"); and Blawas et al., 1998, *Biomaterials* 19:595 (hereinafter "Blawas"); and U.S. Patent No. 6,129,896 (hereinafter "Noonan"); and U.S. Patent No. 6,210,910 (hereinafter "Walt").

According to the Office, Lam discloses providing a first class of particles in a first reaction vessel and second class of particles in second reaction vessel; forming a mixture of the particles and randomly distributing the particles on a surface and reacting a portion of the mixture with a test substance and acquiring at least one image of the particles. However, with respect to claims 34 and 42, the Office admits that Lam does not teach a first and second optically detectable code to interpret the result of a binding experiment nor at least one flat viewing surface and a shape that self orients the viewing surface to face a viewing direction substantially perpendicular to the surface. With respect to claims 36 and 43, the Office admits that Lam does not teach a transparent portion of a particle. With respect to claims 37 and 44, the Office admits that Lam does not teach fused fibers of various colors, the colors and relative position of the fibers indicating the code. With respect to claims 38 and 45, the Office admits that Lam

does not teach the attachment of biological cells to a particle. With respect to claim 41, the Office admits that Lam does not teach acquiring a set of images at the examination site each image corresponding to different spectral band and using a computer program to identify particles of the same class by using the images to develop a mask for the particles of the same class, and detecting one or more reporting modalities within the mask.

The Office believes that one or more of the other cited references compensates for the deficiencies in Lam and thus believes that the skilled artisan would have been able to combine the disclosures of the cited references at the time of the invention to arrive at the claimed subject matter. The Office concludes that the invention is obvious in view of the cited references. Applicants respectfully disagree.

**A. <u>The Prima Facie Standard</u>**

MPEP § 2143 provides the standard required to establish a prima facie case of obviousness. "First there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references combined) must teach or suggest all the claim limitations."

The motivation to make the claimed invention and the reasonable expectation of success must both be found in the prior art, not the applicant's disclosure. *In re Vaeck*, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). The references must be considered as a whole and must suggest the desirability, and thus the obviousness of making the combination. *Hodosh v. Block Drug Col, Inc.*, 229 U.S.P.Q. 182, 187 n.5 (Fed. Cir.

1986); MPEP § 2141. The Patent and Trademark Office (PTO) bears the burden of initially establishing a prima facie case of obviousness. MPEP § 2142. The PTO has not met its burden in the instant case.

### B. The Suggested Combination Would Not Reasonably Be Expected to Succeed

Claim 41, and its dependencies, recite in part: "each of the particles has at east one flat viewing surface and a shape that self-orients the viewing surface to face a viewing direction." The Office points to Lee, Egner, Blawas, Noonan, and Walt and suggests each of these references disclose this element and alleges other carriers were standard in the art at the time and success could be expected because all four of these secondary references disclose that proteins, peptides, nucleic acids, and antibodies can be attached to these carriers.

Applicants submit that none of these references could be combined with Lam, with any reasonable expectation of success as suggested by the Office, and thus that the claims are not prima facie obvious.

#### 1. Lee

The Office tries to suggest that the flat tag allegedly disclosed by Lee could be translated into the particle having at east one flat viewing surface and a shape that self-orients the viewing surface to face a viewing direction. Applicants disagree. The tag in Lee serves as a label: "An improvement in the known method of tagging individual units of production of a substance with microparticles for retrospective identification is disclosed" (Abstract). The claimed particle is not itself a tag. Moreover, the Lee tag is visually decoded with a microscope or other magnifying device (Abstract). But the claim recites "attaching a first type of analyte to particles in the first vessel, and attaching a

second type of analyte to particles in the second vessel." It would be impossible to decode the Lee tag as it is described if an analyte were attached to it. The analyte would interfere with the ability to decode using a microscope or magnifying device as suggested by Lee.

**2. Noonan**

The Office tries to suggest that the flat chip allegedly disclosed by Noonan could be translated into the particle having at east one flat viewing surface and a shape that self-orients the viewing surface to face a viewing direction. Applicants disagree. The alleged flat surfaces of Noonan comprise fibers "bundled in a predetermined arrangement." "The bundled fibers are fused together to fix their predetermined arrangement. Finally, the bonded fiber bundle is sliced into a plurality of individual devices or chips." Noonan states that the fibers are bonded together using biologically inert bonding adhesives such as polysulfone. The biologically inert bonding medium fills the interstices intermediate the plurality of fibers thereby separating the functional moieties on the plurality of fibers." (Noonan, column 3, lines 1-9). The Noonan "chips" thus primarily comprise inert adhesive material and thus could not have a first or second optically detectable code as recited in the claims. No optically detectable code is disclosed in Noonan. Moreover, the Noonan "chips" are all uniform and the instant claim recites: "a first class of particle in a first vessel, each particle in the first class having a first optically detectable code, and a second class of particles in a second vessel, each particle in the second class having a second optically detectable code." It is unclear how a first and second class of particles could be made using Noonan's method.

### 3. Blawas

Blawas is a review article that describes various types of protein patterning. The Office believes Blawas discloses a flat viewing surface as claimed. A skilled artisan reading Blawas at the time of the invention however would find no reasonable assurance of success regarding any type of multiplexed experiment described by Blawas. Blawas begins by stating: 'While each of these methods may be useful for some applications, each has its inherent limitations, particularly in the areas of multiple protein binding, non-specific binding, and in the ability to immobilize proteins while retaining their maximum activity" (page 595, 1st column, 1st paragraph). Blawas continues: "Work in the area of three-dimensional protein patterning has focused on developing components for a biological three dimensional working circuit, generally referred to as a biochip. The actual means for construction of such a circuit are theoretical, if not speculative" (page 597, 1st column, 2nd paragraph). Blawas goes on to discuss significant problems with all the described coupling chemistries used for the attachment of proteins (pp 602-603, e.g., "the most apparent disadvantage is the effect of the patterning technique on the overall protein activity." "A concern with the photochemical techniques is the limited ability to control the surface energy of the background region." "The most difficult aspect using photochemical methods is that the surfaces are sensitive to UV light." "The primary disadvantage with arylazide, bensophenone and diazirine chemistries as they have been applied to protein patterning is that the protein must be in intimate contact with the derivatized surface during the irradiation process, and therefore there is potential for reduction in protein activity by UV light." "One disadvantage is that the surface must be prepared ahead of

time, and the protein solution is incubated in a single step, this discourages the possibility of multiple protein patterning. The only means for binding multiple proteins would have to involve alkanes with selectively pendant groups that would only bind a single protein in a specific manner." "For large scale arrays of proteins, peptides or oligonucleotides many of the techniques discussed suffer from the need for repeated processing steps." "The most difficult issue to address for protein patterning is non-specific binding (NSB) of protein to surface....The problem is only further compounded when patterning multiple proteins, because more than one protein may be present within a given region."

The Office is reminded of its obligation to consider the cited reference as a whole. A skilled artisan considering all that Blawas teaches would conclude that the protein patterning disclosed by Blawas is fraught with difficult problems, many of which remain unresolved, and thus reasonable expectation of success is hardly assured.

**4. Walt**

The Office tries to suggest that the optic fiber well allegedly containing at least one flat surface disclosed by Walt could be translated into the particle having at least one flat viewing surface and a shape that self-orients the viewing surface to face a viewing direction. Applicants disagree. The optic fiber wells disclosed by Walt are all uniform. All that distinguishes one well from another is the analyte and the label. The claim recites something different i.e., a first and second class of particle. Thus, relying on Walt, there would be no reasonable expectation of succeeding in making a "first class of particle" and "a second class of particle" as the claim recites. Moreover, it is not clear how an optic fiber containing a well could be distributed randomly on an

examination surface (as recited by the claim) or why a skilled artisan would be motivated to do so.

**5. Egner**

The Office alleges that Egner discloses a flat shape with two substantially parallel planar sides instead of the round shape of the bead (Office Action dated August 11, 2006, page 6). Applicants believe Egner only describes the use of beads and submit that they could not find the disclosure of a flat surface in Egner. Accordingly, Applicants call upon the Office to point to a particular paragraph or figure in Egner where this may be found or alternatively withdraw the rejection.

**C. The Combined References Do Not Teach of Suggest All of the Claim Limitations**

Turning next to claim 41 and its dependencies, the Office alleges that the combined references of Lee, Egner, Blawas, Noonan, and Walt teach the use of a computerized sensor array for randomly detecting a mixed population of cells where each individual cell is encoded with a single fluorophore or chromophore or ratio of such dyes and positioned in an optically addressable microwell. The Office believes that the identity and location of each cell type is determined by the characteristic optical response of the dye and the apparatus for the optical detection of the cells includes instruments such as an epifluorescence microscope and CCD camera where the data is processed by a computer using image processing software.

Claim 41 recites in part: "operating a computer program to identify particles of the same class by using the images to develop a mask for the particles of the same class, and detecting one or more reporting modalities within the mask." The Office has pointed to nothing in any reference of record that teaches or suggests using the images to

develop a mask for the particles of the same class, and detecting one or more reporting modalities within the mask. Accordingly, the cited references do not teach or suggest all of the claim limitations, and thus claim 41 and its dependencies are not prima facie obvious.

For each of the reasons set forth above, Applicants submit that none of the pending claims are prima facie obvious. Applicants respectfully request withdrawal of the rejection.

## II. Conclusion

In view of the foregoing remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims. Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account.

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on January 10, 2007.

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Respectfully submitted,

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